Is There a Role for Acute Vasoreactivity Testing Outside of Patients With Pulmonary Arterial Hypertension?

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The Ask the Expert column highlights challenges faced in caring for patients with pulmonary arterial hypertension (PAH). In this issue, Richard Krasuski, MD, comments on the role of acute vasoreactivity testing (AVT) in the heart failure population.

Recent guidelines have identified acute vasoreactivity testing (AVT), assessment of drop in pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR) with administration of short-acting pulmonary vasodilator agents such as inhaled nitric oxide, as an important component of the initial hemodynamic evaluation in patients with pulmonary arterial hypertension (PAH).[1,2] Although AVT has traditionally been utilized to identify patients with idiopathic PAH who may be candidates for calcium channel blocker therapy,[3,4] our group and other investigators have demonstrated that AVT response also provides independent prognostic information that may extend to other WHO Group I PH patients (PAH) and even those with non-Group I pulmonary hypertension.[5-7] Many studies are currently exploring the potential role of PAH-targeted therapy in these extended patient populations, including those patients with left sided cardiac abnormalities, the subject of this issue of *Advances*. Interestingly, many of the therapies currently approved for PAH were initially studied in patients with left ventricular (LV) systolic dysfunction, with disappointing multicenter trial results leading to their abandonment.[8,9] Effort was not made, however, to select patients with elevated PVR in these studies.

In applying AVT among WHO Group 2 PH patients, the potential for a dynamic increase in left heart filling pressure needs to be recognized. This phenomenon is not clearly understood but is thought to suggest underlying, pervasive diastolic dysfunction (DD), which may be accentuated when potentially protective pulmonary vasoconstriction is overcome. The hemodynamics for such an example are provided in Figure 1. In this case an elderly woman with a dilated cardiomyopathy and mild to moderate mitral regurgitation was optimized on medical therapy, but remained clinically limited (New York Heart Association function class III) and was referred for hemodynamic evaluation of pulmonary hypertension. She was empirically started on a course of sildenafil, which was discontinued due to clinical worsening. Her baseline pressures obtained at cardiac catheterization (Figure 1A; PAP 72/28 with mean of 42 mm Hg and a mean pulmonary capillary wedge pressure [PCWP] of 14 mm Hg with calculated PVR of 6.5 Wood units) initially suggested a significant component of pulmonary arterial disease and a potential role for pulmonary vasodilator therapy. During inhalation of 40 ppm of nitric oxide (Figure 1B), however, the patient's mean PCWP increased to 30 mm Hg with V-waves to 65 mm Hg (no significant change in PAP and drop in PVR to 1.8 Wood units), suggesting either worsened mitral regurgitation or significant LV compliance issues. When nitric oxide was stopped (Figure 1C), the pressures returned to baseline within seconds. These findings potentially explain why sildenafil had been poorly tolerated, and eventually led to further exploration of her valvular dysfunction and augmented treatment with systemic vasodilators.

Although the understanding of LV systolic dysfunction has transitioned from a hemodynamic to a neuro-hormonal model, management of the "congested" patient remains strongly grounded in hemodynamic principles with a continued role for tailored-management utilizing agents that improve clinical outcomes. A subset of patients, however, will continue to experience functional limitations despite optimal therapy. In some of these patients, elevated PVR may be contributing, but how to identify the patients who benefit from agents targeting the abnormal PVR remains controversial. The use of AVT prior to the initiation of targeted PAH therapy may offer insight into the predominant problem before instituting a potentially detrimental treatment. Current guidelines caution against widespread adoption of targeted PAH therapy in non-PAH patients for fear of provoking fluid retention and pulmonary edema, as well as lack of data to support its use to date.[1] To facilitate a clearer future understanding, thorough hemodynamic assessment, which may include AVT in appropriate patients, should become an essential component in the heart failure population.

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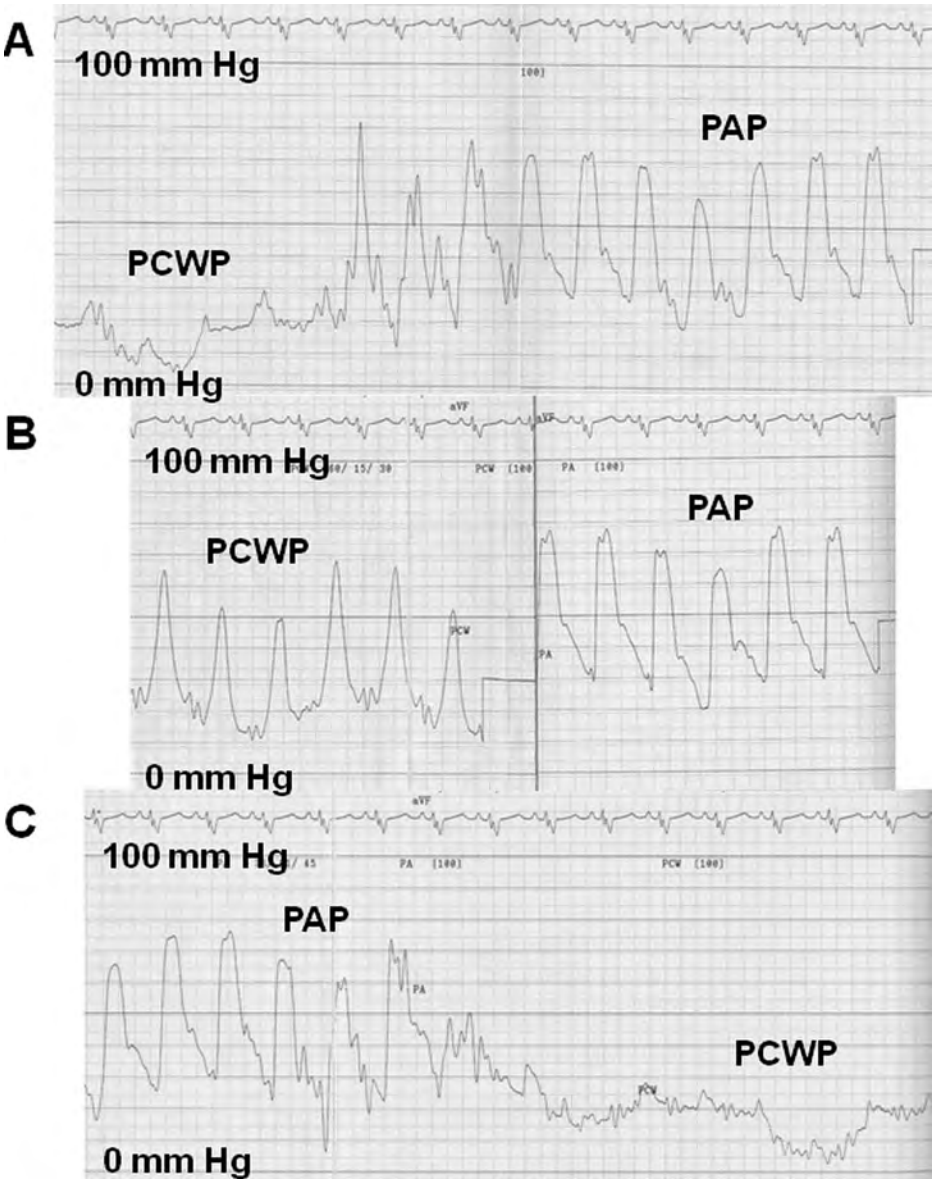

Figure 1: Hemodynamic tracings obtained during catheterization of a 78-year-old woman with a dilated cardiomyopathy, ejection fraction of 25%, and 2+ mitral regurgitation by echocardiography. The latter also showed a dilated right ventricle, 3+ tricuspid regurgitation, and an estimated right ventricular systolic pressure of 70 mm Hg. In Panel A the baseline hemodynamics are demonstrated including PCWP and PAP. The patient then inhaled 40 ppm of nitric oxide with 100% oxygen for 5 minutes with repeat hemodynamics shown in Panel B. This showed profound increases in the PCWP despite minimal effects on PAP. When nitric oxide administration was aborted, the pressures returned nearly back to baseline in under a minute (Panel C). PAP = pulmonary arterial pressure; PCWP = pulmonary capillary wedge pressure.

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